REMARKS

A restriction requirement under 35 U.S.C. §§121 and 372 was set forth in the Official Action dated August 8, 2007 in the above-identified patent application.

At the outset, it is noted that a shortened statutory response period of one (1) month was set forth in the August 8, 2007 Official Action. Therefore, the initial due date for response was September 8, 2007. A petition for a one (1) month extension of time is presented with this response, which is being filed within the one month extension period.

It is the Examiner's position that claims 1-38 and 42-52 in the present application are now drawn to nine (9)patentably distinct inventions which are as follows:

Group I: Claim(s) 1-8, 44, drawn to a nucleic acid sequence having a p66shc coding sequence, including a sequence encoding a mutant p66shc molecule as well as a vector/expression system comprising said nucleic acid sequence, a cell transformed with the vector, a method of producing a modified p66shc polypeptide and a polypeptide encoded by the sequence of claim 1.

Group II: Claim(s) 9, 10, 12, 19, 20-25, 27, 36, 37, 46-52, drawn to a method of modulating resistance in cells to oxidative stress by disrupting the p66shc signal transduction pathway in a cell, said method comprising the step of contacting said cell with an agent capable of modulating p66shc expression wherein the agent is a nucleic acid molecule capable of hybridizing to nucleic acid encoding p66shc thereby reducing or preventing p66hsc expression wherein the agent is administered for the treatment of a disease.

Group III: Claim(s) 9, 12-17, 22, 27, 36, 44, 48, 49, 52,

drawn to a method of modulating resistance in cells to oxidative stress by disrupting the p66shc signal transduction pathway in a cell wherein the step of disrupting p66shc affects the susceptibility of p66shc to phosphorylation, wherein said step of disrupting p66shc causes a mutant p66shc polypeptide to be expressed or affects the ability of a kinase to phosphorylate p66shc, wherein the method is for the treatment of a disease.

Group IV: Claim(s) 9, 12, 18, 22, 26, 27, 36, 38, 48, 49, 52, drawn to a method of modulating resistance in cells to oxidative stress by disrupting the p66shc signal transduction pathway in a cell, said method comprising the step of contacting said cell with an agent that is an antibody that specifically binds p66shc polypeptide thereby disrupting its function, wherein the agent is administered for the treatment of a disease.

Group V: Claim(s) 9, 11, 28, 29, 31, 44, 45, drawn to a method of modulating resistance in cells to oxidative stress by affecting the p66shc signal transduction pathway in a cell, said method comprising the step of contacting said cell with an agent capable of modulating p66shc expression wherein the agent is a vector comprising a nucleic acid encoding p66shc wherein the agent is administered for the treatment of a disease.

Group VI: Claim(s) 9, 28-30, drawn to a method of modulating resistance in cells to oxidative stress by affecting the p66shc signal transduction pathway in a cell, said method comprising the step of contacting said cell with an agent capable of modulating p66shc expression wherein the agent is a transcription factor wherein the agent is administered for the treatment of a disease.

Group VII: Claim(s) 32-35, 44, drawn to a method of screening for compounds capable of modulating resistance in cells to oxidative stress comprising contacting a candidate compound with a p66shc expression system and determining the amount of a compound of the signaling pathway and comparing said amount of said component with the amount in the absence of the compound.

Group VIII: Claim(s) 42, drawn to a method of determining the presence or absence of p66shc nucleic acid or a mutant, variant derivative or allele thereof in a biological sample, comprising the step of contacting said sample with a nucleic acid molecule capable of hybridizing specifically with said p66shc nucleic acid or a mutant, variant derivative or allele thereof and determining whether or not hybridization has taken place.

Group IX: Claim(s) 43, drawn to a method of determining the presence or absence of a p66shc polypeptide or a mutant, variant derivative or allele thereof in a biological sample, comprising the step of contacting said sample with an antibody binding domain capable of binding p66shc thereof and determining whether or not binding has taken place.

The Examiner notes that claims 1-8 are generic to the species of p66shc mutants and that claims 12 and 17 are generic to the species of kinases.

Should Applicants elect any of the Groups II- VII inventions, the Examiner has required that Applicants further elect a particular disease to be treated. At the outset, claims 27 and 52 have been amended to recite the disease of "vascular complications of diabetes". Support for this

amendment can be found at page 19, line 27 of the application.

If Group I is elected, Applicants must select a single p66shc mutant for examination on the merits. Finally, if Group III is elected, Applicants must select one of the kinases encompassed by the claims.

The Examiner further contends that Groups III, IV and VII encompass patentably distinct species and if any of these groups are elected, the Examiner has required applicants to elect a single species from these groups for examination on the merits. Following such an election, Applicants must also indicate which claims read on the elected species.

At the outset, Applicants are dismayed that the Examiner has chosen to restrict the present application further despite Applicants strenuous traversal of the initial requirement for restriction. Applicants continue to respectfully disagree with the Examiner's position and submit that a withdrawal, or at the very least a modification of the instant restriction requirement is clearly in order for the following reasons.

Applicants again respectfully submit that during the international stage of this application the PCT Examiner did not make a lack of unity finding and considered all of the claims to be directed to a single invention. Plainly, the instant restriction requirement again fails to comply with the established United States Patent and Trademark Office practice of following the international rules regarding unity of invention in the prosecution of applications filed under §371. While the Examiner purports to employ the general inventive concept practice under PCT Rule 13.1, it is wholly unclear how the Examiner could conclude that the instant application has nine (9) Groups of inventions, when the PCT Examiner, employing the same rules, determined that identical claims in the international application have **complete unity** of invention. Accordingly, Applicants respectfully request the instant restriction requirement be withdrawn and all of the

claims be examined on their merits.

The present invention relates to the inventive concept that $p66^{shc}$ acts in a pathway that regulates stress response. This was not recognized anywhere in the art and constitutes a significant contribution to the art. The Examiner cites Migliaccio et al. as an anticipatory reference. However, these investigators wholly fail to appreciate the role p66shc modulation plays in the oxidative stress response. Accordingly, it cannot be reasonably maintained that the disclosure in this reference anticipates the subject matter of the present claims.

Moreover, Applicants submit that placement of claims 9. 10, 12, 19, 20-25, 27, 36, 37, and 46-52 of Group II and claims 9, 11, 28, 29, 31, 44, and 45 of the Group V invention into separate groups of invention is wholly improper. Clearly, claim 9 is generic to the Groups II and V inventions at the very least. Group II is directed to a method of modulating resistance to oxidative stress by disrupting p66 signaling pathway via introduction of an nucleic acid which hybridizes to p66shc. The Group V claims are directed to a similar method wherein the agent is a vector comprising a nucleic acid a nucleic acid encoding p66shc. A restriction requirement is only considered proper if there would be a serious burden on the examiner if restriction were not required (see MPEP §808). As groups II and V both relate to a method of modulating resistance in cells to oxidative stress and the vector of group V contains nucleic acid that is at least structurally related to the nucleic acid of group II (albeit not necessarily identical), searching and examining the claims in group V, as well as those in group II, would not impose an undue search burden on the Examiner. In particular, when searching the subject matter of the claims of group II, it is clear that the examiner would also necessarily search subject matter relating to the claims of group V.

Thus, at least the claims of Groups II and V inventions clearly relate to the same inventive concept, i.e., the participation of $p66^{shc}$ in a pathway that regulates stress response. Accordingly, Applicants respectfully request withdrawal of the restriction requirement between these groups of claims. Indeed, all of claims of the Groups II and V inventions expressly refer to methods of modulating resistance in cells to oxidative stress by modulating the $p66^{shc}$ signal transduction pathway.

Thus, at the very least, Applicants submit that the pending claims must be considered to relate to a common inventive concept (namely, the involvement of $p66^{shc}$ in the oxidative stress response pathway). Accordingly, Applicants request that the restriction requirement be withdrawn between the groups II and V inventions at the very least.

In order to be fully responsive to the instant restriction requirement, Applicants hereby elect, with traverse, Group II, namely claims 9, 10, 12, 19, 20-25, 27, 36, 37, 46-52 drawn to a method of increasing resistance in cells to oxidative stress. As mentioned above, claims 27 and 52 have been amended to recite "vascular complications of diabetes". Applicants further elect vascular complications of diabetes as the disease to be treated. It is submitted that each of the claims in the Group II and Group V inventions read on the elected disease.

Applicants' election in response to the present restriction requirement is without prejudice to their right to file one or more continuing applications, as provided in 35 U.S.C. §120, on the subject matter of any claims finally held withdrawn from consideration in this application.

Early and favorable action on the merits of this

application is earnestly solicited.

Respectfully submitted,
DANN, DORFMAN, HERRELL AND SKILLMAN
A Professional Corporation

By 
Kathleen D. Rigaut, Ph.D., J.D.
PTO Registration No. 43,047

Telephone: (215) 563-4100
Facsimile: (215) 563-4044
Email: krigaut@ddhs.com